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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,377	07/06/2005	Valerie Autier	MERCK-3028	8732

23599 7590 05/29/2008

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
HUGHES, ALICIA R	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
05/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,377	AUTIER ET AL.	
	Examiner	Art Unit	
	Alicia R. Hughes	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,27,28 and 30-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16, 27-28, and 30-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 16, 27-28, and 30-46 are pending and the subject of this Office Action. Applicant cancelled claims 1-15 and 17-21 in the response filed on 02 November 2007.

Applicants' arguments filed on 02 November 2007 have been fully considered and are, in part, deemed to be persuasive regarding the previous rejection. Rejections not reiterated from this Office's previous action are hereby withdrawn. The rejections set forth herein constitute the complete set of rejections being applied to the instant application presently.

Claim Rejections - 35 U.S.C. §112.2

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

First 112, Second Paragraph Rejection

Claims 40-43 are rejected under 35 U.S.C. 112, second paragraph, for indefiniteness.

Claim 40 is drawn to "a prodrug of one of the following compounds." The term "prodrug" is a relative term which renders the claim indefinite. In particular, "prodrug" does not particularly point out the degree or type of derivation that a given compound may have in relation to the parent compound and still be considered a "prodrug" as intended by Applicants. Applicants have failed to provide any specific definition for this term in the present specification. Lacking such a definition, the skilled artisan would not be reasonably apprised of the metes and

bounds of the subject matter for which the Applicants seek patent protection. Rather, a subjective interpretation of the claimed language would be required. However, as such is deemed inconsistent with the tenor and express language of 35 U.S.C. §112.1, second paragraph, the claims are deemed properly denied.

Second 112, Second Paragraph Rejection

Claims 36-39 and 44-46 are rejected under 35 U.S.C. 112, second paragraph, for indefiniteness. The claims recite the limitation "[a] method according to claim 34." There is insufficient antecedent basis for this limitation in the claims, because claim 34 is not drawn to a method, but rather to a composition.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16, 27-28, and 30-46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14, 28-29, 33, and 55-56 of U.S. Patent Application No. 10/541,493. Although the conflicting claims are not identical, they are not patentably distinct from each other, because they contain overlapping/closely related subject matter, most notably, the treatment of diabetes and related complications by administering to a patient in need thereof a kynurenine 3-hydroxylase inhibitor.

Applicant has noted that the '493 application does not teach or suggest the specific compounds in the present set of claims and therefore, the obvious-type double patenting rejection should be withdrawn. To the contrary, it is well-understood in art that an obvious-type double patenting rejection does not require anticipation, but rather, a show of a *prima facie* case of obviousness, which has been established based on the administration of a kynurenine 3-

hydroxylase inhibitor, and some with the same core structure as claimed in the instant application.

In view of the foregoing, the above rejection is proper.

Claim Rejections – 35 U.S.C. §103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

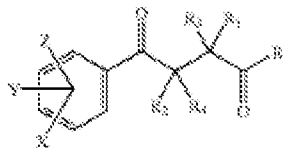
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16, 27-28, and 30-46 are rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,323,240 B1 [hereinafter referred to as "Giordani et al"] in view of U.S. Patent No. 6,572,542 [hereinafter referred to as "Houben et al"].

Giordani et al teach a class of 4-phenyl-4-oxobutanoic acid derivatives and their pharmaceutically acceptable salts (Abstract) with a core structure that encompasses the core structure of the present invention useful in the treatment of glaucoma/retinopathy (Col. 3, lines 4-20). Giordani et al also teach that the 4-phenyl-4-oxobutanoic acid derivatives are used as a kynurenine-3-hydroxylase inhibitor (Col. 3, limes 4-5). It is well understood in the art that retinopathy is a known complication associated with diabetes. (Houben et al, Col. 1, lines 38-67; *see also* Diabetes Research Foundation, "Diabetes and Your Eyesight," printed from http://www.glaucoma.org/learn/diabetes_and_yo.html, 2 pages).[1]

More specifically, as with the present invention, Giordani et al disclose the following

> Accordingly, the present invention provides a 4-phenyl-4-oxo-butanoic acid derivative of formula (I) either as a single isomer or as mixture of isomers
>
> (I)
>
> 
>
> wherein
>
> X, Y and Z are, each independently, hydrogen, halogen, cyano, nitro, C_1–C_6 alkyl, phenyl, benzyl, C_2–C_6 alkenyl, C_2–C_6 alkynyl, C_1–C_6 alkoxy or C_1–C_6 alkylthio;
>
> R is hydroxy; —OR_5 in which R_5 is C_1–C_6 alkyl, phenyl, benzyl, C_2–C_6 alkenyl or C_2–C_6 alkynyl; —$N(R_6)_2$ or —$N(R_6)OR_6$ in which each R_6 is, independently, hydrogen, C_1–C_6 alkyl, C_2–C_6 alkenyl, C_2–C_6 alkynyl, phenyl or benzyl;
>
> R_1, R_2, R_3 and R_4 are, each independently, hydrogen, halogen, hydroxy, thiol, C_1–C_6 alkoxy, C_1–C_6 alkylthio, C_1–C_6 alkyl, C_2–C_6 alkenyl, phenyl or benzyl, or
>
> R_1 and R_2 or R_2 and R_3 together form a group =CHR_6 in which R_6 is hydrogen, a straight C_1–C_5 alkyl chain or phenyl;

(Col. 2, lines 38-67) and

[1] Cited on previous PTO-892 form.

In the present invention, R^1 may represent a heterocyclic radical, which could be identical to the phenyl ring disclosed in Goirdani et al. The present invention's R^2 is the equivalent of Giordani's R^2, and the present invention's R^3 is the equivalent of Girodani's R^4. According to Giordani, both its R^2 and R^4, just as its R^3 and R^1, can be hydrogen, halogen, thiol, alkenyl, alkoxy, etc., just as the present invention's R^2 and R^3 positions can be the same. The present invention's W represents a divalent radical which is the equivalent to the cycloalkyl formed in Giordani et al that includes R^1 and R^3, and finally, R^4 in the present invention, which is the equivalent of R in Giordani et al, can both be, for example, a heterocyclic ring or an alkenyl or alkyl.

In light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art to utilize the administration of a 4-phenyl-4-oxobutanoic acid derivatives used as a kynurenine-3-hydroxylase inhibitor as a method of treating diabetes and associated complications.

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR of Public PAIR. Status information for unpublished applications is available through Public PAIR only. For information about the PAIR system, see http://pair-direct-uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alicia R. Hughes/
Examiner, Art Unit 1614
/Raymond J Henley III/
Primary Examiner, Art Unit 1614